

Appl. No. 09/887,569

Response dated January 9, 2004

Reply to Final Office Action of August 12, 2003

Remarks

The office action dated May 4, 2004 has been carefully considered. It is believed that the following comments and amendments represent a complete response to the Examiner's objections and place the present application in condition for allowance. Reconsideration is respectfully requested.

35 USC §102

The Examiner has maintained his objection to claims 17, 20 and 23-24 as being anticipated by Upjohn (WO 91/13993) under 35 USC §102(b). We respectfully disagree with the Examiner for the reasons that follow.

The present applicant was the first to achieve the expression of recombinant somatotropin in seed. Applicant prepared somatotropin as a fusion protein that allowed the expression and accumulation of the somatotropin in seed. Prior to the present invention, the prior art expressed a desire to achieve the expression of somatotropin in seed although no one was successful in achieving that result. The reference cited by the Examiner, Upjohn, is an example of a prior reference that state the desirability of expressing somatotropin in seed. However, the reference does not provide an enabling disclosure that would allow one of skill in the art to express somatotropin in seed.

Upjohn suggests the expression of somatotropin in seed but also does not demonstrate that they were able to produce significant levels of somatotropin in seed. Upjohn describes preparing somatotropin as a fusion with a seed storage signal peptide which is cleaved soon after expression. In this regard, we refer to page 20, lines 11-16 of Upjohn:

"The polypeptide resulting from expression from these fused gene is expected to initially include the seed storage signal peptides, which should be removed as a

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result of normal proteolytic cleavage to yield a Bst polypeptide which would be identical to the naturally occurring peptide except for the presence of two to four additional amino acids at its N-terminus."

In contrast, in the present invention, somatotropin is expressed as a fusion protein that is not cleaved but rather accumulates as a fusion protein in the seed as is demonstrated in Example 1 and Figure 2.

The Examiner maintains that "accumulates" has not been defined with regard to the duration of accumulation or the amount of accumulated product. Webster's online dictionary (www.webster-dictionary.org) defines accumulate as "To heap up in a mass; to pile up; to collect or bring together; to grow or increase in quantity or number". The Applicant submits that while Upjohn suggests the expression of somatotropin in seed, they do not demonstrate that they were able to produce significant levels of somatotropin in seed. Furthermore, if one were to assume that the somatotropin did accumulate, Upjohn indicates in Example 10, page 20, lines 11-16 that the polypeptide resulting from expression from these fused genes is expected to initially include the seed storage signal peptide, which should be removed as a result of normal proteolytic cleavage. Therefore, if one were to assume that accumulation had occurred, the protein product that accumulated did not contain the signal peptide and did not accumulate as a fusion protein in the plant seed.

In view of the foregoing, we respectfully request that the objections to the claims under 35 USC §102(b) be withdrawn.

35 USC §103

The Examiner has objected to the claims 17, 20 and 23-25 under 35 USC §103(a) as being unpatentable over Upjohn (WO 91/13993) in view of Vandekerckhove et al. We respectfully disagree with the Examiner for the reasons that follow.

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As stated previously, Upjohn does not disclose or even suggest the production of somatotropin as a stable fusion protein that accumulates in the seed. In fact, Upjohn teaches away from the present invention as it discloses that the expression of a phaseolin signal peptide fused to a somatotropin and the signal peptide is cleaved by normal proteolytic cleavage. As a result, there is no motivation in Upjohn to prepare somatotropin as a fusion protein that is not automatically cleaved after expression. The deficiencies in Upjohn are not remedied by Vandekerckhove *et al.* Vandekerckhove *et al.* is not concerned with the expression of somatotropin in seed. The Examiner has previously stated that Bosch *et al.* reinforces a reasonable expectation of success when using a signal sequence which targets the protein product "to a plant compartment where proteins are stably accumulated", such as the seed storage protein sequence taught by Vandekerckhove *et al.* It should be noted that the Bosch *et al.* proposed solution above is not applied by Vandekerckhove *et al.* Vandekerckhove *et al.* teaches the insertion of leuenkephalin, a pentapeptide, into the entire 2S albumin gene and not just a signal sequence. Furthermore, Vandekerckhove *et al.* uses the leuenkephalin pentapeptide as they express concerns about expressing a larger protein. The pentapeptide is used due to the fact that the small size should have minimal disruption of the protein structure (see Vandekerckhove *et al.* page 929, second column, first full paragraph). Therefore, a person of ordinary skill in the art would have no expectation of success when combining Upjohn and Vandekerckhove *et al.*

The Examiner has objected to the claim 30 under 35 USC §103(a) as being unpatentable over Upjohn (WO 91/13993) in view of Vandekerckhove *et al.* as applied to claims 17, 20 and 23-25 and further in view of Orlikowska *et al.* We respectfully disagree with the Examiner for the reasons that follow.

Claim 30 relates to a specific embodiment of the invention wherein the plant seed is safflower. As a result, these claims carry with them all of the novel and inventive features of Claim 1 from which this claim depends. Our comments on the Upjohn and Vandekerckhove *et al.* references appear above and equally apply to this claim. The

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deficiencies in the Upjohn and Vandekerckhove *et al.* references are in no way remedied by Orlikowska *et al.* Orlikowska *et al.* is a reference that describes the effects of co-cultivation on transformation efficiency and shoot regeneration of safflower. Orlikowska *et al.* in no way teaches or suggests the expression of somatotropin in seeds.

The Applicant maintains that the solution for successful accumulation of somatotropin in a plant seed is to accumulate somatotropin as a fusion protein.

In view of the foregoing, we respectfully request that the objections to the claims under 35 USC §103(a) be withdrawn.

The Commissioner is hereby authorized to charge any fee (including any claim fee) which may be required to our Deposit Account No. 02-2095.

In view of the foregoing comments, we respectfully submit that the application is in order for allowance and early indication of that effect is respectfully requested. The Examiner is kindly requested to contact the undersigned by telephone at (416) 957-1682 at his convenience should there be any issues to discuss.

Respectfully submitted,

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